IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Wilson et al.

Serial No.: 09/478,737 Examiner: Murphy

Filed : January 6, 2000 Group Art Unit: 1646

For : SCREENING METHODS FOR COMPOUNDS USEFUL IN THE TREATMENT OF POLYCYSTIC KIDNEY DISEASE

RULE 131 DECLARATION

I hereby certify that this paper is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on:

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Carmella L. Stephens
Attorney Name

41,328
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Carmella L. Stephens
Signature

June 9, 2004
Date of Signature

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, PATRICIA D. WILSON, do declare:

1. I am a co-inventor, with Dr. Christopher Burrow, of the invention disclosed in the above identified patent application. A copy of my Curriculum Vitae is attached herewith as Exhibit A.

2. Claims 21-23 of the above identified patent application are directed to a method for identifying a compound capable of modulating polycystin-1 mediated increased cell adhesion to type I collagen coated substrates (Exhibit B).

4. Attached herewith as Exhibit C, is a Memorandum dated **September 25, 1998,** which was sent to Dr. Brian Kelly of the Mount Sinai Medical Center Technology Transfer Office describing a cell adhesion based method for drug screening. As set forth in the Memorandum, a cell line expressing polycystin-1, *i.e.*, human renal epithelial cells (step 1), could be used in cell adhesion assays on type I collagen (step 2), to identify compounds that change the number of clusters formed (step 3).

5. As evidenced by Exhibit C, the cell adhesion assay encompassed by claims 21-23 of the above identified patent application was developed prior to April 27, 1999, the publication date of the van Adelsberg publication entitled "Peptides from the PKD Repeats of Polycystin, the PKD1 Gene Product, Modulate Pattern Formation in the Developing Kidney" (see, Exhibit D).

6. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of any patent issuing from the above-captioned patent application.

Date: 6/4/04

Dr. Patricia D. Wilson

CURRICULUM VITAE

PATRICIA D. WILSON
Division of Nephrology
Department of Medicine
Mount Sinai School of Medicine
1425 Madison Avenue, Rm 11-23
New York, NY 10029
Phone 212-659-9383
Fax 212 849 2434
E-mail Pat.Wilson@mssm.edu

ACADEMIC APPOINTMENTS:

1982-1985	Assistant Professor of Medicine & Microbiology, University of Colorado Health Sciences Center, Denver, CO.
1985-1992	Associate Professor Physiology, UMDNJ-Robert Wood Johnson Medical School (Formerly Rutgers Medical School), NJ.
1986-1989	Assistant Director, Graduate Program in Cell and Developmental Biology, Rutgers University, NJ.
1992-1996	Associate Professor of Medicine & Physiology, The Johns Hopkins University School of Medicine, Division of Nephrology, Baltimore, MD.
1996-1999	Associate Professor of Medicine, Mount Sinai Medical Center, New York NY.
1999-Present	Professor of Medicine, Mount Sinai Medical Center, New York, NY.
2000-Present	The Irene and Dr. Arthur Fishberg Professor of Medicine (Nephrology).

EDUCATION:

University of Nottingham, Nottingham, England	B.Sc. (Honours)	1966	Zoology
London University, England	Ph.D	1973	Cell Biology

POSTDOCTORAL TRAINING:

1973-1978	Postdoctoral Research Fellowship, Imperial Cancer Research Fund, London, England.
1978-1979	Medical Research Council Fellow, Clinical Research Centre, London, England.
1980-1982	Physiology Institute, University of Munich, Deutsche Forschungsgemeinschaft Fellow, Munich, Germany.

HONORS:

1976	Invited participant to organize the establishment of European collaborative research program on "Cellular aging and the decreased capacity of organs."
1976-1979	Chairman of the "Liver Group" of the European Community concerted action on Aging (Eurage).
1977	Wellcome Foundation Travel Award, Prof. M.J. Karnovsky, Harvard Medical School, Dept. of Pathology, Boston, MA.
1979-1980	Leukemia Research Fund Award, Clinical Research Center, London, England.
1979	Guest Research Fellow at the Pathologisches Institut der Universitaet Muenchen.
1980	Guest worker at the Sidney Farber Cancer Institute, Boston, Dr. Lan Bo Chen.
1982-Present	American Society of Nephrology, Chairman and abstract reviewer
1994	American Society Nephrology Organizing Committee
1997-2000.1	Newman Research Fellow: Mount Sinai School of Medicine, Department of Medicine.
1997-Present	Elected member Salt and Water Club
2000-Present	The Irene and Dr. Arthur Fishberg Professor of Medicine (Nephrology), Mount Sinai School of Medicine (endowed chair).
2001-Present	Premedical Research Student Advisory Council
2002-Present	New York Academy of Science Research Training Mentor

INVITED LECTURES: (SELECTED)

1989	"Polarity Abnormalities in Autosomal Dominant Polycystic Kidney Disease". American Society of Cell Biology; St. Louis, Missouri.
1990	"Cell Biology of Polycystic Kidney Disease". State-of-the-Art Lecture, European Concerted Action on PKD.
1991	"Cell and Molecular Biology of ADPKD". State-of-the-Art Lecture , Advances in Nephrology.
1992	"The Role of Epithelial Cell Polarity and Hyperplasia in ADPKD". NIH Conference on Genetic Diseases: Reston, Virginia.
1992	Proteases in Renal cell Injury. ISN Forefronts in Neprhology.
1992	"Cyst Formation in Polycystic Kidney Disease". NIDDK Conference Molecular Genetics of Kidney Diseases.
1993	"Autosomal Dominant Polycystic Kidney Disease". Johns Hopkins University of Medicine Biennial.
1993	"Renal Proteases in Cellular Injury". XIIth International Society of Nephrology; Jerusalem, Israel.
1994	"Abnormalities in Polarized Molecular Transport in PKD Cyst Epithelia". ISN Forefronts in Nephrology; Niagara-on-the-Lake, Ontario, Canada.
1994	"Polycystic Kidney Disease". State-of-the-Art Lecture, European Society of Pediatric Nephrology; Amsterdam, The Netherlands.
1994	"Pathogenesis of Polycystic Kidney Disease". European Concerted Action on Polycystic Kidney Disease; Leiden, The Netherlands.
1995	"Renal Cystic Disease: Cell Biology of ADPKD", NIH.
1995	"Renal Cystic Disease": International Symposium of Progression of Chronic Renal Disease.
1995	"Gene Expression in ADPKD": International Workshop on Developmental Renal Physiology.
1995	"Polarization of Epithelia in Nephrogenesis": International Pediatric Nephrology Association.

1995 Pathogenesis of Autosomal Dominant Polycystic Kidney Disease: Molecular Medicine Institute, Oxford England.

1995 Molecular pathogenesis of polycystic kidney disease. The Mayo Clinic.

1995 The Dunaway Burnhma Visiting Professor of Physiology address: Epithelial Polarity Defects in Autosomal Dominant Polycystic Kidney Disease. Darmouth Medical School.

1996 "Polycystin": Basic Science Conference of American Society Nephrology, on Renal Developmental Biology.

1997 "Expression of the PKD-1 Protein in Human Normal and ADPKD Epithelia": Fourth International Workshop on Polycystic Kidney Disease. Leiden, The Netherlands.

1998 "Molecular Pathophysiology of Autosomal Dominant Polycystic Kidney Disease: Function of the PKD-1 Encoded Protein". University of Alabama.

1997 European Pediatric Nephrology Conference, Keynote Speaker: "Renal Cyst Formal During Development".

1999 FASEB Symposium Keynote Speaker: "Modifications of EGF Receptor Polarized Distribution During Development".

1998 International Society Nephrology: Renal Development Symposium, Keynote Speaker: "Gene Differentiation and Cyst Formation".

1999 American Society Nephrology: Invited Speaker Clinical Science Symposium: "Polycystic Kidney Diseases: New Insights into Pathogenesis and Therapy:" Polycystin: New Aspects of Structure, Regulation and Function.

1999 Fifth International Workshop on PKD: Invited Symposium Speaker: Function of the Polycystin-1 Protein.

2000 NIH Workshop: Mucolipin, TRPs and Human Disease: Invited Symposium Speaker; "Multiprotein Complexes Containing Polycystin-1, -2 and TRP- Related Proteins".

2001 American Society Pediatric Nephrology. Invited Symposium Speaker: "Polycystin: Kidney Development and PKD"

2003 London University Matrix Group, Imperial College, London, England . " Polycystin-1, the PKD1 Gene Product, Functions and a Matrix Receptor"

PROFESSIONAL SOCIETIES:

1966-1980	Royal Microscopical Society, London
1966-1981	British Society for Cell Biology
1968-1982	European Society for Cell Biology
1970-1980	European Concerted Action on Aging: Founder Member Liver Group
1982-1985	American Federation for Clinical Research
1985-1991	American Society for Gerontology
1985-Present	New York Academy of Science
1997-2000	American Heart Association
1982-Present	American Society of Nephrology
1982-Present	American Association for the Advancement of Science
1982-Present	American Society for Cell Biology
1996-Present	American Physiology Society
1997-Present	American Society for Developmental Biology

REVIEW PANELS AND STUDY SECTIONS:

1984-Present	NSF ad hoc
1984-Present	VA
1988-Present	NIH: ad hoc for RFAs, reviewer reserve
1988-Present	NIH: Site Visit Teams for NIDDK, NIEHS
1991-Present	Kidney Foundation of Canada
1992-1997	Polycystic Kidney Research Foundation grant review committee
1992-1996	NIH: General Medicine B Study Section
1997-2000	National Kidney Foundation
1997-Present	March of Dimes
1997-Present	NIH: Special Review Committee, chairman
1999-2001	New York/New Jersey chapter of National Kidney Foundation
2000-2002	NIH: Cardiovascular and Renal Study Section
2000-Present	Human Frontier Science Program
2002-Present	Kidney and Urological Society
2002-Present	Wellcome Foundation, England
2003-present	NIH: NIDDK-D study section

ADVISORY BOARDS AND ORGANIZING COMMITTEES:

1992-1997	Scientific Advisory Board, Polycystic Kidney Research Foundation.
1993	Advisory Committee for 6th International Workshop on Developmental Renal Biology.

1994	American Heart Association: Advisory Committee: Renal Development.
1994-1995	Program Committee: the Sixth International workshop on Developmental Nephrology, Airlie House, Virginia. Organizer, Symposium "Maldevelopment of the Kidney and Urinary Tract".
1994	American Society of Nephrology Nominating Committee.
1994-1995	American Society of Nephrology Program Committee
1994-1995	International Workshop on Developmental Renal Physiology
1994-1995	Advisory Committee: International Symposium on Progression of Chronic Renal Disease.
1994-1995	Organizer, Symposium "Control of Growth and Differentiation": International Pediatric Nephrology Association.
1996-Present	Director of pre- and post-doctoral research: Department of Medicine, Division of Nephrology, Mount Sinai School of Medicine.
1997-1998	American Society Nephrology Nominating Committee
1997-Present	Scientific Advisory Board: Devgen Biotechnology Company
2000-2001	Salt and water club, New York organizer
2000-2001	8th International Workshop on Developmental Nephrology, organizer
2001-Present	Advisory Council: Premedical Research Opportunities Program Mount Sinai School of Medicine
2002-Present	Medical Advisory Board: Medifocus Inc.

JOURNAL PEER REVIEW ACTIVITIES:

Science
Nature
Nature Genetics
Trends in Physiological Sciences
Proceedings of the National Academy of Sciences
Journal American Society Nephrology
American Journal of Physiology: Cell
American Journal of Physiology: Renal
Journal of Clinical Investigation
American Journal of Pathology
Lancet
Laboratory Investigation
Journal of Cellular Physiology
Pediatric Nephrology
Kidney International
American Journal of Kidney Diseases
Gerontology
Journal of Laboratory and Clinical Medicine
Toxicology and Applied Pharmacology
Journal Histochemistry & Cytochemistry

OTHER PROFESSIONAL APPOINTMENTS:

1992-1994	Department of Medicine Steering Committee
1992-1994	Subcommittee on Industrial Funding
1992-1996	Basic Science Security Committee
1994-1996	Department of Medicine: Women's Task Force: Divisional Representative
1996-Present	Director of Students, Department of medicine, Division Nephrology
1997-1998	Chairman, Department of Medicine User Group
1999-Present	Mount Sinai Medical Center Industrial Liaison Advisor and Patent Review Committee
2000-Present	Appointments and Promotions Committee: Basic Science
2000-2001	Chairman, Departmental (Urology) Review

TRAINING RECORD:

Post-doctoral Fellows

Michel Burnier, M.D.	1983-1985	Assistant Professor, University Zurich, Switzerland
Ann C. Sherwood, Ph.D.	1987-1991	Assistant Professor, UMDJH-Robert Wood Johnson Medical School
Patricia A. Hartz. Ph.D.	1988-1993	Instructor, Johns Hopkins School of Medicine
Ping Xia, Ph.D.	1988-1991	Instructor, University Calgary, Canada
Doris Falkensteing, Ph.D.	1992-1994	Assistant Professor, Campinas University
Eudora Eng, M.D.	1993-1995	Fellow, Johns Hopkins University School of Medicine
Olivier Devuyst, M.D.	1994-1996	Nephrologist and Physician/Scientist, University
Deborah Hyink, Ph.D.	1995-Present	Post-doctoral Fellow, Mount Sinai School Medicine
Zheng Gu, M.D.	1996-1997	Nephrologist, Shanghai Second Medical University
Xiaohong Li, Ph.D.	1997-Present	Post-doctoral Fellow Mount Sinai School Medicine
Lin Geng, Ph.D.	1997-1999	Instructor, Mount Sinai School Medicine
Hsi-Ping Li, Ph.D.	1997-2000	Instructor, Mount Sinai School Medicine
William Gans, M.D.	2000-2001	Urology Resident, Mount Sinai School Medicine
James Borin, M.D.	2001-2002	Urology Resident, Mount Sinai School Medicine
Michael Levin, M.D.	2002-2003	Urology Resident, Mount Sinai School Medicine

Graduate Students

Jing Du	1988-1992, Ph.D.	Staff Scientist, NIH, Bethesda, MD
Ning-Tsu Kuo	1988-1992, Ph.D.	Instructor Case Western Reserve University
Robin Hammell	1988-1992, Ph.D	Post-doctoral Fellow UMDNJ-Robert Wood Johnson
Mita Gangopadhilly	1990-1991	Masters Student UMDNJ-RWJ Medical School, NJ
Libo Qiu	1996-2001, M.D.	Pathology Resident, Mount Sinai Medical School
Andrew Greenberg	2000-2001	Medical Student, Grenada Medical School
Sirisha Chalasani	2000-2001, M.D.	Resident, Internal Medicine Eastern PA
Marc Handlesman	2001	
Padmaja Garangaraj	2001, M.D.	Resident Atlantic City Hospital, NJ
Sherin John	2002-present, M.D.	

Undergraduate Students

Katie Palla	(Rutgers University)	1989-1991
Laura Gatti	(Rutgers University)	1991-1993
Cindy Wong	(Princeton University)	1996
Katie Thornton	(Hunter College)	1996-1997
Rebecca Zausmer	(Barnard University)	1997-Present
Lillian Kang	(NYU at Buffalo)	1998-1999
Luke Riservato	(Vassar University)	1999
Alexander Lavy	(Williams College)	1999-2000
Bhavi Hansoty	(Vassar University)	2000
Michael Esrick	(Vassar University)	2001
Henry Brown	(Touro College)	2001
Grace Kwon	(CUNY)	2001
Varun Verma	(NYU)	2002
Connie Yee	(NY Acad Science)	2002-Present
Daisy Condua	(Lehigh University)	2002
Sharon Israeli	(Mount Sinai/NYU)	2003-present

Medical Students

Katy Thornton	(Mount Sinai)	1997-1998
Kit Chang	(Mount Sinai)	1998-2001
Emad Yacob	(Mount Sinai)	1998
Melissa Taylor	(Necker, Paris)	1998
Adam Graziano	(Mount Sinai)	1999
Svetlana Sionova	(Mount Sinai)	1999-2000
Jay Mueller	(Mount Sinai)	1999-2000
Alex Chan	(Mount Sinai)	2001
Sherry Megalla	(Mount Sinai)	2002
Hilda Fernandez	(Irvine, Doris Duke Fellow)	2002-2003

TEACHING ACTIVITIES:

1982-1985	University of Colorado, Health Sciences: Physiology (renal fellows) Cell Biology (renal fellows)
1985-1992	Rutgers University and Robert Wood Johnson Medical School: Renal Physiology (1^{st} year medical students) General physiology seminars (1^{st} year medical students) Cell and Developmental Biology (graduate students)
1992-1996	Johns Hopkins University and School of Medicine Renal Physiology Seminars (1^{st} year medical students) Developmental Biology Seminars (1^{st} year medical students) Nephrology Seminars (renal fellows)
1996-Present	Mount Sinai School of Medicine Nephrology Core curriculum, renal physiology and Seminars (renal fellows) Renal Pathophysiology (2^{nd} year medical students)
1997-Present	Fellows Molecular and Cellular Techniques Course

GRANT SUPPORT:

Past Grants

1972-1982	Chronic granulocytic leukemia: Leukemia Research Fund, England 1979 PI: P. Wilson (100%); 30,000 pounds sterling
1984-1985	Knoll Parmaceuticals: Effect of calcium channel blocking drugs on ischemic injury renal cells: Pi: P. Wilson, (5%) $12,000
1985-1990	Co-PI (25%) of NIH Program Project (PI: P. Gabow): Pathogenesis of Autosomal Dominant Polycystic Kidney Disease; $154,000
1985-1988	Co-PI (25%) of NIH Program Project (PI: R. Schrier) Cellular Mechanisms of Ischemic and Neprhotoxic Injury: $168,000
1987-1991	Co-PI (20%) NIH RO1: Toxicity of Cyclosporine Metabolites
1985-1992	PI: P.Wilson (30%): NIH RO1: Effects of Aging on Renal Epithelial Cells; $45,000
1989-1999	PI: P. Wilson (30%) NIH RO1: Mechanisms of Cyst Formation in Human Polycystic Kidney Disease $485,000
1986-1996	PI: P. Wilson (25%) NIH RO1: Epithelial Polarity Defects in ADPKD $989,000
1991-1995	Co-PI (15%): NIH RO1 (PI: E. Avner): Cellular Biology of Congenital Murine Cystogenesis ($32,000)
1994-1995	PI: P. Wilson (10%) Merck: Renal Toxicity of Merck Immunosuppressive in Cultured Human Renal Epithelial Cells: $151,000
1994-1996	Co-PI (10%) Genentech (PI: C.R. Burrow): Purification of NB-GF $50,953
1994-1995	Sponsor NIH NRSA: Transcription Factors in Human Renal Differentiation (E. Eng, Postdoctoral Fellow, $120,000)
1994-1995	Sponsor PKRF Reseaerch Grant: Role of Pax02 in Polycystic Kidney Disease (E.

	Eng, Postdoctoral Fellow, $25,000)
1996-1999	Sponsor NIH NRSA: Molecular Control of Renal Epithelial Differentiation (Postdoctoral Fellow D.Hyink, Ph.D. $90,000)
1998-2001	Sponsor American Heart Association, Scientist Development Award Structure Function Analysis of the Autosomal Dominant Polycystic Kidney Disease Gene Product, Polycystin. (Post-doctoral Fellow/Instructor) L.Geng M.D., Ph.D. $260,000
1998-2001	Sponsor NIH NRSA. Sturcture-Function Analysis of ADPKD Gene Products (Post-doctoral Fellow, L. Geng, M.D., Ph.D.) : F32 09778-01 $96,000
1999-2001	Sponsor American Heart New Investigator Award. Phosphorylation and Functional Significance of the C-Terminal Domain of the PKD-1 Encoded Protein (Instructor, H. Li, M.D., Ph.D. $26,000)
1999-2000	Sponsor; National Kidney Foundation Fellowship Award (NY/NJ). Molecular Function of the ADPKD Assoociated PRKX Family of Serine Protein Kinases. (Post-Doctoral Fellow, X. Li, M.D., Ph.D. $25,000)
1988-2000	NIH RO1: Mechanisms of Cyst Formation in Human Polycytic Kidney Disease $453,881
1996-2000	NIH Program Project Grant: PI: P. Klotman. Molecular Therapy for Renal Disease (P. Wilson, Co-PI, 10%) $398,797
1997-2001	NIH RO1: R. Abramson PI: Molecular Basis of Renal Urate Transport. (P. Wilson, Co-PI 10%)
1999-2001	DeVgen Biotechnology Company: Mammalian Epithelial Cell Biology of PKD Pathway: Validation of Potential Molecular Targets of Potential Therapeutic Importance. P. Wilson, PI (5%) $196,538; 1999-2001
1990-2003	NIH RO1: Epithelial Polarity in Autosomal Dominant Polycystic Kidney Disease. P. Wilson, PI $1,007,734 1990-2003
1999-2003	NIH KO1 Role of Retinoids in Renal Cell Specification Deborah Hyink, Ph.D , Mentored Research Scientist Development Award: P. Wilson Sponsor $83,350

Current Grants

NIH PO1	Design of Novel Therapeutic Strategies for Polycystic Kidney Diseases P. Wilson PI $1,000,000 2003-2008
NIH P01:	Pathogenesis of HIV-Associated Nephropathy. P. Wilson Co-PI $209,609 1999-2004
Vistagen Biotech:	Proteomic Analysis of Human Renal Epithelial Cell Toxicity. P. Wilson, PI $101,250 2000-2004
NIH NRSA	Role of Serine/Threonine Protein Kinases in ADPKD $37,500, 2001-2004 Xiaohong Li, M.D.,Ph.D, National Research Service Award P. Wilson Sponsor $43,800 2001-2004

PUBLICATIONS:

Original Peer-Reviewed Articles

1. Wilson, P.D. Electron microscopic demonstration of two types of mitochondria with different affinities for lead. *Histochem J.*, **1**:405-416, 1969.

2. Maggi, V., Franks, L.M., Wilson, P.D., Carbonell, A.W. Localization of insulin in mouse tissues using fluorescence microscopy and light microscope and high resolution autoradiography. *Diabetologia.*, **5**:67-78, 1969.

3. Franks, L.M., Wilson, P.D. "Spontaneous" neoplastic transformation *in vitro* the ultrasturcture of the tissue culture cell. *Europ. J. Cancer*, **6**:517-523, 1970.

4. Wilson, P.D., Franks L.M. Enzyme patterns in young and old mouse kidneys. *Gerontologia*, 17:16-32, 1971.

5. Wilson, P.D. Enzyme patterns in young and old mouse livers and lungs. *Gerontologia*, **18**:36-54, 1972.

6. Wilson, P.D., Franks, L.M. The ultrastructure of tumors derived from spontaneously transformed tissue culture cells. *Br.J. Cancer*, **16**:380-387, 1972.

7. Wilson, P.D. Reversible and irreversible effects of tissue culture on enzyme patterns of spontaneous mouse tumors and mouse and human embryo tissues. *Cancer Res.*, **33**:375-382, 1973.

8. Wilson, P.D. Enzyme changes during aging. Z. *Alternforsch*, **27**:353-367, 1973.

9. Wilson, P.D. Enzyme patterns in non-neoplastic and spontaneously transformed tissue culture cells: a histochemical and biochemical study. *J. Pathol.*, **114**:21-28, 1974.

10. Wilson, P.D. Characterization of spontaneous and induced epithelial and mesenchymal tumors by their enzyme patterns. *J. Pathol.*, **113**:151-159, 1974.

11. Franks L.M., Wilson, P.D., Whelan, R.D. The effects of age on total DNA and cell number in the mouse brain. *Gerontologia.*, **20**:21-6, 1974.

12. Wilson, P.D., Franks, L.M. The effect of age on mitochondrial ultrastructure. *Gerontologia*, **21**:81-94, 1975.

13. Wilson, P.D., Franks, L.M. The effect of age on mitochondrial ultrastructure and enzymes. *Adv. Exp. Med. Biol.*, **53**:171-183, 1975.

14. Wilson, P.D., Hill, B.T., Franks, L.M. The effect of age on mitochondria enzymes and respiration. *Gerontologia*, **21**:95-101, 1975.

15. Wilson, P.D., Franks, L. M. Alkaline phosphate in mitochondria. *Cell. Biol. Int. Rep.*, **1**:85-92, 1977.

16. Wilson, P.D., Benham, F., Franks, L.M. Alkaline phosphatase phenotypes in tumour and non-tumour cell lines: not an invariable marker for neoplastic transformation.*Cell Biol Int. Rep.*, **1**:229-38, 1977.

17. Benham, R., Cottell, D.C., Franks, L.M., Wilson, P.D. Alkaline phosphatase activity in human bladder tumor cell lines. *J. Histochem. Cytochem.* **25**:266-274, 1977.

18. Wilson, P.D., Summerhayes, I.C., Franks, L.M. Alkaline phosphatase as a marker of transformation in adult mouse bladder epithelium after *in vitro* exposure to 7,12 dimethylbenz(a)anthracene. *Cell Biol Int. Rep.*, **2**:365-74, 1978.

19. Wilson, P.D. Differential enzyme distribution in lobules of livers from young and old mice and rats. *Gerontology*, **24**:348-374, 1978.

20. Rustin, G.J.S., Wilson, P.D., Peters, T.J. Studies on the subcellular localization of human neutrophil alkaline phosphatase. *J. Cell. Sci.*, **36**:401-412, 1979.

21. Wilson, P.D., Hodges, G.M. Focal distribution of surface marker enzymes after long-term culture of adult rat bladder epithelium and methyl nitrosourea (MNU)-induced bladder tumors. *J. Histochem. Cytochem.*, **27**:1236-1246, 1979.

22. Wilson, P.D., Rustin, G.J.S., Peters, T.J. The ultrastructural localization of human neutrophil alkaline phosphatase in normal individuals during pregnancy and in patients with chronic granulocytic leukaemia. *Histochem. J.*, **13**:31-43, 1981.

23. Wilson, P.D. Electron microscopic cytochemical localization of nucleoside phosphatase in normal and chronic granulocytic leukemic human neutrophils. *Histochem. J.*, **13**:73-84, 1981.

24. Wilson, P.D., Summerhayes, I.C., Hodges, G.M., Trejdosiewicz, L., Nathrath, W.J. Cytochemical markers of bladder carcinogenesis. *Histochem. J.*, **13**:989-1007, 1981.

25. Nathrath, W.J., Wilson, P.D., Trejdosiewicz, L.K. Immunohistochemical demonstration of epithelial and urothelial antigens at light and electron microscope levels. *Acta Histochem.*, **25**(Suppl): 73-82, 1982.

26. Wilson, P.D. Lieberman, E.L., Peters, T.J. Ultrastructural localization of adenosine diphosphatase in cultured aortic endothelial cells. *Histochem. J.* **14**:215-219, 1982.

27. Wilson, P.D., Watson, R., Knook, D.L. Effects of age on rat liver enzymes: a study using isolated hepatocytes, endothelial and Kupffer cells. *Gerontology*, **28**:32-43, 1982.

28. Horster, M.F., Wilson, P.D. Nephron epithelia in culture: growth of loop of Henle cells in hormonally defined serum-free media. *Cell. Bio. Intern. Rep.*, **5**:765-666, 1982.

29. Nathrath, W.B.J., Wilson, P.D., Trejdosiewicz, L.K. Immunohistochemical localization of keratin and luminal epithelial antigen in myoepithelial and luminal epithelial cells of human mammary and salivary gland tumors. *Pathol. Res. Prac.*, **175**:279-288, 1982.

30. Wilson, P.D., Nathrath, W.B., Trejdosiewicz, L.K. Immunoelectron microscopic localization of keratin and luminal epithelial antigen in normal and neoplastic urothelium. *Pathol. Res. Prac.*, **175**:289-298, 1982.

31. Nathrath, W.B., Arnholdt, H., Wilson, P.D. Keratin, luminal epithelial antigen and carcinoembryonic antigen in human urinary bladder carcinomas. An immunohistochemical study. *Pathol Res Pract.* **175**:299-307, 1982.

32. Wilson, P.D., Brouwer, A., DeLeeuw, A.M. Enzyme properties of Kupffer and endothelial cells. In: *Sinusoidal Liver Cells*; Knook, D.L., Wisse E. (Eds), pp 499-501, 1982.

33. Wilson, P.D., Horster, M.F. Differential response to hormones of defined distal nephron epithelia inculture. *Am J Physiol.*, **244**:C166-74, 1983.

34. Wilson, P.D., Smith, G.S., Peters, T.J. Pyridoxal-5- phosphate: a possible physiological substrate for alkaline phosphatase in human neutrophils. *Histochem. J.*, **15**:257-264, 1983.

35. Linke, R.P., Nathrath, W.B., Wilson, P.D. Immunoelectron microscopic identification and classification of amyloid in tissue sections by the postembedding protein-A gold method. *Ultrastruct. Pathol.*, **4**:1-7, 1983.

36. Horster, M.F., Wilson, P.D., Gundlach, H. Direct evaluation of fluorescence in single renal epithelial cells using a mitochondrial probe (DASPMI). *J. Microsc.*, **132**:143-148, 1983.

37. Horster, M.F., Wilson, P.D., Schmolke, M., Kuhner, D. Cell culture and differentiate properties of nephron epithelial cells in defined medium, In: *Hormonally defined media*; Fischer, G., Wieser, R.J. (eds); New York, Springer-Verlag, pp. 347-350, 1983.

38. Wilson, P.D., Watson, R., Breckon, R., Van Beezooijn: Cellular effects of meclofenoxate in livers of young and old rats. In: *Pharmacological, Morphological and Physiological Aspects of Liver Aging.* Van Bezooijen CFA (ed); Eurage: Rijswijk, pp.175-180, 1984.

39. Trejdosiewicz, L.K., Wilson, P.D., Hodges, G.M. A species cross-reactive membrane-associated urothelial differentiation antigen (UMA). *J. Natl. Cancer Inst.*, **72**:355-366, 1984.

40. Horster, M., Brechtelsbauer, H., Wilson, P.D., Schmolke, M. Effects of nicotine on epithelial nephron cells in culture. *Klin. Wochenschr.*, **62**(Suppl. II):86-91,1984.

41. Wilson, P.D., Dillingham, M.A., Breckon, R., Anderson, R.J. Defined human renal tubular epithelia in culture: growth, characterization, and hormonal response. *Am J Physiol.*, **248**:F436-F443, 1985.

42. Wilson, P.D., Horster, M.F. Histochemical localization of hormone sensitive adenylate cyclase in defined nephron epithelia in culture. *Histochemistry*, **82**:539-545, 1985.

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Pending Claims 21-23

21. A method for identifying a compound capable of modulating polycystin-1 mediated increase in cell adherence to type I collagen coated substrate, comprising;

(a) contacting a test compound to a cell expressing a polycystin-1 protein wherein expression of said polycystin-1 protein results in an increase in cell adherence to type I collagen coated substrate;

(b) measuring cell adherence to type I collagen coated substrate; and

(c) comparing the level of cell adherence to type I collagen coated substrate obtained in (b) to the level of cell adherence to type I collagen coated substrate obtained in the presence of a vehicle control:

wherein a decrease in the level of cell adherence to type I collagen coated substrate obtained in (b) compared to that obtained in the presence of a vehicle control, indicates indemnification of a compound capable of modulating polycystin-1 activity.

22. The method of Claim 21 wherein the cell is recombinantly engineered to express a mutant polycystin-1 protein.

23. The method of Claim 21 wherein the polycystin-1 protein is overexpressed wherein over expression of the polycystin-1 protein results in an increase in cell adherence to type I collagen coated substrate.

Mount Sinai

The Mount Sinai Medical Center
One Gustave L. Levy Place
New York, NY 10029-6574
FAX (212) 987-0389

Division of Nephrology
Box 1243

Paul E. Klotman, M.D.
Chief

Ruth G. Abramson, M.D.
Leslie A. Bruggeman, Ph.D.
Christopher R. Burrow, M.D.
Basil G. Hanss, Ph.D.
Thomas Kahn, M.D.
Deepak M. Kaji, M.D.
Marvin F. Levitt, M.D.
Joseph J. Lieber, M.D.
Michael S. Lipkowitz, M.D.
Barbara T. Murphy, M.D.
Edgar Leal-Pinto, M.D.
Richard M. Stein, M.D.
Avelino V. Teixeira, Ph.D.
Jaime Uribarri, M.D.
Patricia D. Wilson, Ph.D.
Jonathan A. Winston, M.D.
Guofeng You, M.D.

MEMORANDUM

FROM: **P. Wilson, Ph.D, Christopher Burrow, M.D.**

TO: **Brian Kelly, Ph.D**

DATE: **September 25th, 1998**

RE: **Cluster-Formation Assay for ADPKD Drug Screening**

PROPOSED CLUSTER-FORMATION ASSAY FOR DRUG SCREENING

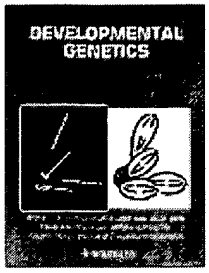
The assay consists of:

1. The culture of human renal epithelial cell lines from normal and autosomal dominant polycystic kidney disease (ADPKD) origin [ORIGINATED BY PW 1985/86 and PW/CRB 1995: IN PUBLIC DOMAIN]

2. The use of these cells in an adhesion assay : 4 hours on type I collagen; which induces formation of clusters containing specific sets of proteins [DESCRIBED IN PUBLICATION UNDER REVIEW AT PRESENT]

3. The use of these cells in the screening of potential drugs by determination of quantitative changes in numbers of clusters formed and the composition of the clusters. Mutant cells make larger numbers of clusters after a 4 hour time frame and the clusters are deficient in a protein (focal adhesion kinase, FAK). The assay would screen for cluster formation by numbers (immuno-fluorescence techniques with antibody developed by PW/CRB lab) and by content of FAK. THE USE OF THIS SYSTEM TO SCREEN FOR DRUGS IS COMPLETELY NOVEL AND HAS NOT BEEN PRESENTED PREVIOUSLY AND WILL NOT BE PRESENTED IN THE PUBLICATION UNDER REVIEW OR IN ANY OF THE PRESENTATIONS AT THE MEETINGS IN OCTOBER.

Our feelings are that Devgen's request for exclusive licensing rights to the assay be given serious consideration. Based on our current understanding of the issues we favor this as long as there was a clause that if they decided not to use it we would not be prevented from using it ourselves or offering it to others.



Developmental Genetics
Volume 24, Issue 3-4 , Pages 299 - 308
Published Online: 27 Apr 1999

Research Article

Peptides from the PKD repeats of polycystin, the PKD1 gene product, modulate pattern formation in the developing kidney

Janet van Adelsberg *

Department of Medicine, Columbia University, New York, New York

email: Janet van Adelsberg (jsv1@columbia.edu)

*Correspondence to Janet van Adelsberg, Department of Medicine, Columbia University, 630 West 168th Street, P&S 10-501, New York, NY 10032.

Funded by:
- March of Dimes Foundation; Grant Number: FY98-0153
- American Heart Association, Established Investigatorship

Keywords

kidney development; branching morphogenesis; polycystic kidney disease; image analysis

Abstract

Mutations in the *PKD1* gene cause the majority of cases of autosomal dominant polycystic kidney disease. The *PKD1* gene codes for a protein of unknown function, polycystin-1, that is predicted to be a receptor. Its large extracellular domain contains 16 copies of novel motif, the PKD repeat, that is likely to be a ligand binding domain based on its similarity to immunoglobulin domains. These observations suggested that soluble fragments of the extracellular domain of polycystin-1 could be used as competitive inhibitors of polycystin function in a suitable model system. Polycystin-1 is highly expressed in the ureteric bud and other branching epithelia during development and interacts with β-catenin, a molecule known to play a role in branching morphogenesis. These data suggested that polycystin-1 might play a role in branching morphogenesis. I show here that peptides derived from the PKD repeats of polycystin-1 caused an asymmetric pattern of ureteric bud branching in cultured kidney rudiments. Treatment of kidney rudiments with experimental but not control peptides reduced both the number of ureteric bud branches and the number of nephrons. Experimental peptides produced significant morphogenetic effects at concentrations ≤0.1 mM. These data suggest that polycystin-1 plays a role in branching morphogenesis by the ureteric bud. Dev Genet 24:299-308, 1999. © 1999 Wiley-Liss, Inc.

Received: 12 October 1998; Accepted: 16 December 1998